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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,787	PASCUAL, DAVID W.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,27-36 and 55-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,27-36 and 55-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/12/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/19/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed July 17, 2006. Applicant's response to restriction requirement of June 16, 2006 has been entered. No new claims have been added or amended and no claims have been cancelled.

Claims 1-64 are pending in the application.

Election/Restrictions

Applicants' election of Group I (claims 1-11, 27-36 and 55-63, without traverse, drawn to a composition comprising M cell specific ligand, a nucleic acid encoding an immunogen, and a nucleic acid binding moiety, and a method of using said composition as a vaccine to immunize a host, is acknowledged.

Claims 12-26, 37-54 and 64 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions. The requirement for restriction is deemed proper, maintained and hereby made FINAL.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Applicant timely responded to the restriction (election) requirement in the Paper filed July 17, 2006. Claims 1-11, 27-36 and 55-63 are currently under examination.

Objection to the Specification

The amendment to the specification filed 2/4/2004 is objected to, as being incomplete. The amendment should indicate that U.S. Patent Application No. 10/169,492 is now abandoned, and that U.S. Provisional Application No. 60/174,786 was filed January 6, 2000.

Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 27-36 and 55-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims embrace numerous M cell tropic fragments of reovirus σ1 protein and adhesins derived from Salmonella and polio virus. The specification fails to disclose any examples of said M cell tropic fragments. The specification does not describe the structure or functional nature of any M cell tropic fragments, and simply states that such fragments are also contemplated by the invention.

The claims encompass a large number of possible peptides and fragments that may be derived from adhesins of Salmonella and polio virus and the reovirus σ1 protein and tested to determine their respective M cell tropism; and thus constitute a claimed genus that encompasses M cell tropic fragments yet to be discovered. The specification fails to disclose any species of M cell tropic fragments, or provide a description for any structural features of said M cell fragments of the claimed genus. As such, the Artisan of skill could not predict that Applicant possessed any species of M cell tropic fragments.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). Moreover, MPEP 2163 states:

> [A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the

> sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Applicant's attention is also directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Overall, what these statements indicate is that the Applicant must provide adequate description of such core structure and function related to that core structure such that the Artisan of skill could determine the desired effect. Hence, the analysis above demonstrates that Applicant has not determined the core structure for full scope of the claimed genus.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. Therefore, the breadth of the claims as reading on numerous M cell tropic fragments yet to be discovered; in view of the level of knowledge or skill in the art at the time of the invention, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of the genus of M cell tropic fragments. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of numerous M cell tropic fragments, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 7-8, 27-36, 55 and 62-63 are rejected under 35 U.S.C. 102(e) as being anticipated by Brey et al. (U.S. Patent No.: 6,187,335, filed Dec. 31, 1997).

Brey et al. teach methods and materials comprising polymerizable liposomes coupled to ligands which target mucosal tissue, for oral drug delivery of biologically active substances (Title and Abstract). The polymerizable liposomes are described as useful for oral and/or mucosal delivery of vaccines in the form of polymerizable fatty acids coupled to targeting ligands with an affinity for human and mammalian intestinal M cells and similar cells in the nasopharyngeal cavity, such as lectins or proteins or peptides which can bind to M cell, and to polymerizable liposomes incorporating them (column 1). Brey et al. further teach that the targeting ligand is copolymerized with the liposome to form a stable polymerized liposome with the desired targeting ligand covalently attached. The polymerization can be carried out in the presence of a desired therapeutic agent, such as a vaccine or antigen (column 10). A wide variety of therapeutics may be polymerized with the liposomes that include antifungals, antimicrobials, vaccines, cytokines, interferon, hormones, antibacterial agents and DNA and RNA nucleotides exerting a biological effect when administered to an animal (column 14). Therefore, Brey et al. specifically teach DNA nucleotide therapeutics or agents that are antigens, or immunogens. The polymerized liposomes are additionally described as containing phosphatidyl serine (Abstract), hence in the zwitterionic form, the liposomes further contain a nucleic acid binding moiety. Additionally taught by Brey et al. are different methods and modes of administration to a patient that include oral, sublingual, buccal, rectal, vaginal, intranasal and by scarification. Oral delivery

may be in the form of tablets, capsules, solutions and the like of a dosage unit form. When the liposomes contain an antigen, an adjuvant may be included to enhance the effectiveness of the vaccine. The active immunogenic ingredients of a vaccine formulation are further described as mixed with excipients which are pharmaceutically acceptable and compatible (columns 16 and 17).

It should be noted that a kit and instructions contained therein are not afforded any patentable weight. Therefore by teaching all the limitations of claims 1-2, 7-8, 27-36, 55 and 62-63, Brey et al. anticipate the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, and 55-59 are rejected under 35 U.S.C. §103(a) as being unpatentable over Brey et al. (U.S. Patent No.: 6,187,335, filed Dec. 31, 1997), in view of Compans (US. Patent Publication No.: 2003/0092665, priority date April 30, 1997).

Brey et al. describe methods and materials comprising polymerizable liposomes coupled to ligands which target mucosal tissue, for oral drug delivery of biologically active substances (Title and Abstract). The polymerizable liposomes are described as useful for oral and/or mucosal delivery of vaccines in the form of polymerizable fatty acids coupled to targeting ligands with an affinity for human and mammalian intestinal M cells and similar cells in the nasopharyngeal cavity, such as lectins or proteins or peptides which can bind to M cell, and to polymerizable liposomes incorporating them (column 1). Brey et al. further teach that the

targeting ligand is copolymerized with the liposome to form a stable polymerized liposome with the desired targeting ligand covalently attached. Brey et al. state that the therapeutics may be polymerized with the liposomes that include DNA and RNA nucleotides exerting a biological effect when administered to an animal (column 14). Therefore the nucleic acid binding moiety is represented by polymerizable liposomes. Brey et al. do not teach a liposome vaccine composition that further comprises a nucleic acid binding moiety that is a polypeptide.

Compans describes methods and compositions comprising nucleic acid molecules encoding an antigen formulated with an bioadhesive agent to improve adherence and uptake of the nucleic acid molecules by cells following their administration to mucosal surfaces (Title and Abstract). Compans further describes carriers for enhanced delivery and immunogenicity of the nucleic acids that include liposomes (paragraph [0040], p. 5) in combination with polycationic compounds that include polylysine (paragraph [0040], p. 6). Compans et al. specifically describe the conjugation of DNA with polylysine in Example 8 (p. 9). It is noted that Example 2 of the instant application teaches the preparation of fusion protein σ1-polylysine DNA complex by utilizing a chemical reaction to covalently link the lysine residues to purified protein σ1.

Therefore, a person of ordinary skill in the art would have been motivated to combine the liposome/polylysine mediated antigen delivery method of Compans et al. with the liposome mediated ligand targeted antigen delivery method of Brey et al., as both compositions and methods involve the delivery of nucleic acid antigens to M cells in mucosal surfaces. A person of ordinary skill in the art, having combined the liposome/ nucleic acid antigen, ligand targeted composition of Brey et al. with the liposome/polylysine nucleic acid antigen composition of Compans would be able to specifically target M cells (as taught by Brey et al.) and enhance nucleic acid antigen delivery and uptake, resulting in an enhanced immune response, with a reasonable expectation of success.

Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine the compositions of Brey et al. and Compans at the time of the instant invention.

Claims 9-10, and 60-61 are rejected under 35 U.S.C. §103(a) as being unpatentable over Brey et al. (U.S. Patent No.: 6,187,335, filed Dec. 31, 1997), in view of Compans (US. Patent

Publication No.: 2003/0092665, priority date April 30, 1997) as applied to claims 1, 3-6, and 55-59 above, and further in view of Rubas et al. (J. Microencapsul. 7:385-395).

While neither Compans or Brey et al. teach M cell specific ligands that include the σ1 protein of a reovirus, Brey et al. state that any protein or peptide ligand that selectively binds to M cells are useful for mucosal application and additionally note that proteolytic processing of reovirus is required for adherence to M cells (column 10), thus providing the motivation to use any M cell specific ligand for targeted delivery of a nucleic acid vaccine, including a protein derived from reovirus.

Rubas et al. describe the incorporation of the reovirus M cell protein sigma 1 into liposomes and showed enhanced selective adherence to M cells, that may be used to facilitate delivery of carrier content and enhancing immune response (Abstract).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to use the σ1 protein of reovirus as the M cell targeting ligand in the compositions of Brey et al and Compans. A person of ordinary skill in the art having combined the mucosal cell delivery composition of Compans with the ligand targeted nucleic acid antigen delivery composition of Brey et al. that included the reovirus σ1 protein as the targeting ligand would have a reasonable expectation of success in specifically delivering a nucleic acid antigen vaccine to an M cell, resulting in the composition and method of the instant invention, with enhanced nucleic acid delivery and immunogenicity.

Conclusion

Claims 1-11, 27-36 and 55-63 are not allowable.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

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PRIMARY EXAMINER